blood cell count increased from 0.4×10^9/L to 1.0×10^9/L in the first 10 days, only to exhibit an accelerated rise afterwards, the count reaching 36.5×10^9/L on the 14th day. G-CSF was therefore discontinued (Fig. 1). The peripheal smear revealed 2% blasts, 3% promyelocytes, 5% metamyelocytes, 14% bands, 58% polymorphonuclear leukocytes, 12% lymphocytes, and 6% normoblasts. Bone marrow aspirate exhibited hypercellularity and marked myeloid hyperplasia (myeloid/erythroid ratio, 8:1), with 1.0% blasts. The white blood cell count declined to 4.6×10^9/L in a period of 8 days. Daily peripheral blood smear examinations revealed the gradual resolution of leukoerythroblastosis. Subsequent bone marrow aspiration was unremarkable except for mild erythroid hyperplasia, with a blast count of 0.5%. On the confirmation of remission, the patient was discharged and was followed as an outpatient on a monthly basis. The patient is well and free of any evidence of relapse after 6 months of follow-up. The exclusion of other possible causes of leukoerythroblastosis such as invasion of the bone marrow with the leukemic clone or infections and the absence of acute hemolysis or sepsis together with resolution of the condition after the discontinuation of treatment have defined G-CSF as the responsible factor for this unexpected finding. After 6 months of follow-up, the patient remains in remission, which can be taken as evidence that leukoerythroblastosis associated with G-CSF administration is a transient and benign condition. We agree with Reykdal et al. [1] that the appearance of blasts may not always indicate relapse, such unexpected effects of G-CSF should always be kept in mind.

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Possible Cytokine Mechanism of Increased Megakaryocytic Proliferation in 5q− Syndrome

To the Editor: We read with interest the excellent article about hematologic features of patients with chromosome 5q deletion by Lewis et al. in the July 1995 issue of the *American Journal of Hematology* [1]. The 5q− syndrome is a clonal hematologic disorder characterized by hypolobulated micromegakaryocytic hyperplasia and a clonal cytogenetic anomaly consisting of an interstitial deletion of the long arm of chromosome 5 (5q−). Increased megakaryocytic proliferation with the characteristic megakaryocyte morphology and the concomitant presence of normal or high platelet counts and leukopenia are from specific features of the 5q− syndrome [1,2].

The proliferation and differentiation of hematopoietic cells is under the control of specific growth factors. Several major hematopoietic growth factors, including interleukin-4 (IL-4), acting on myeloid progenitors are located in the long arm of chromosome 5. On the other hand, the megakaryocytopoietic cytokine IL-6, which seems to be responsible for megakaryocytopoiesis in many cases of reactive thrombocytosis, is located in a different chromosomal location, 7p15 [3,4].

A 32-year-old male patient was admitted to our hospital with the complaints of low-grade fever, malaise, and weight loss. On admission, he had leukopenia (white blood cell count, 1,800/mm^3, with 40% neutrophils in peripheral blood), macrocytic anemia (hemoglobin and mean corpuscular volume, 11.3 g/dl and 92 fl, respectively), and thrombocytosis (platelet count, 996,000/mm^3). Bone marrow examination showed a hypercellular marrow, increased hypolobular micromegakaryocytes, and increased erythroid activity with 10–30% dyserythropoietic precursors. Cytogenetic analysis revealed the 5q deletion breakpoints as (q13:q33). No additional karyotypic abnormality has been found. Serum IL-6 and IL-4 concentrations were 68.3 pg/ml and 0 (undetectable) pg/ml, respectively, in this patient with 5q− syndrome associated with marked thrombocytosis and leukopenia. Normal median serum levels of IL-6 and IL-4, which had been detected in 15 [8 women and 7 men; median age, 26 (range, 24–36)] healthy volunteers with normal platelet counts (range, 191,000–385,000/mm^3), were 5.7 (range, 2.5–21.6) pg/ml and 33.6 (range, 5.1–107.2) pg/ml, respectively, in our enzyme-linked immunosorbent assay laboratory. Therefore, serum IL-6 level was notably increased in this patient with 5q− syndrome while the IL-4 level was found to be significantly decreased.

IL-4 may function directly as a negative regulator of megakaryocytopoiesis and also it inhibits IL-6 synthesis and suppresses IL-6 production in vitro [5,6]. Increased IL-6 concentration in the patient might be due to decreased IL-4 synthesis by reason of the deletion of 5q. IL-6, which has a chromosomal location of 7p15, is a well-known megakaryocyte potentiator [7–9]. Consequently, leukopenia and thrombocytosis in the 5q− patient may be explained by decrease in cytokine interactions by the deletion of the long arm of chromosome 5. Nevertheless, further studies are needed to determine the association between clinical/laboratory hematologic features of patients with chromosome 5q deletion and hematopoietic cytokines.

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Iron Granules in Plasma Cells: A Particular Morphologic Aspect

To the Editor: Iron granules in plasma cells were described in 1938 in a patient with hemochromatosis [1]. They are stained yellow-brown in May-

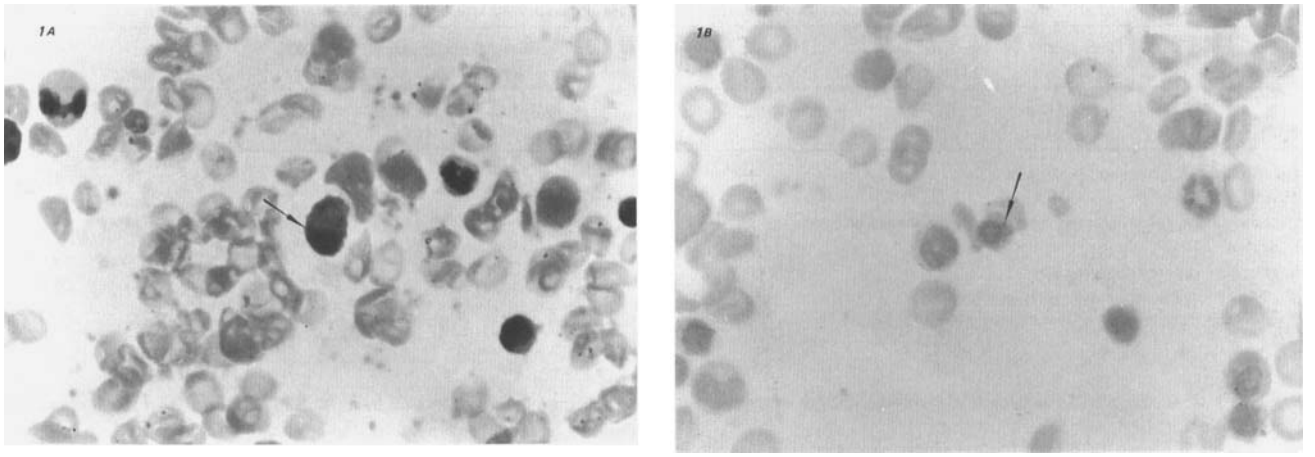

Fig. 1. A: Bone marrow smear stained by the May-Grünwald-Giemsa method. Arrow, iron granule. (High-magnification, ×1,000.) B: Bone marrow smear stained by Perls' Prussian blue and counter-stained with safranin 0.1%. This stain verifies the hemosiderin nature of the granules. Arrow, iron granule. (High magnification, ×1,000.)

Grünwald-Giemsa bone marrow smears (Fig. 1A), but they are blue in Perls' Prussian blue stain with safranin 0.1% counterstain (Fig. 1B).

In 1991 we reported our experience with two male patients, both with excessive drinking habits and macrocytic anemia without megaloblasts; one patient also had liver cirrhosis [2]. Now we report on the presence of iron granules in plasma cells, quantitated as grade 1 [3], in a 91-year-old female patient admitted for anorexia and asthenia. The patient had a previous significant history of breast cancer removed surgically (quadrantectomy). Laboratory tests showed a macrocytic anemia, with mild leucocytopenia. Bone marrow aspiration did not show megaloblastosis. Nodular biopsy on the breast scar showed the presence of neoplastic cells.

We refer to the morphologic aspect because only a few cases have been reported, although the technique employed for identification is easy to use. Both the source of the phenomenon and the causal mechanism are unknown.

It has not yet been determined whether the presence of iron granules in plasma cells could be the expression of a specific nosologic entity.

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Homozygous Thalassemia and Difficult Endotracheal Intubation

To the Editor: Difficulty in airway management constitutes and essential predisposing factor of morbidity and mortality attributable to anesthesia, especially when it is not anticipated preoperatively [1]. With this in mind, we investigated the epidemiological characteristics in difficult endotracheal intubation in regard to the presence of protruding maxilla in homozygous thalassemia patients.

Data were collected in a series of 5,166 anesthetic case records of consecutive adult patients undergoing general anesthesia for routine surgery. Fifteen specialist anesthetists carried out the routine preoperative airway assessment using standardised guidelines. Table I shows eight individual risk factors implicated to cause difficulty in intubation [1–3]. Hypertrophy of the maxilla was defined as forward protrusion of the upper incisors beyond the lower incisors. Anesthesia was induced intravenously; 1 min after administration of succinylcholine 1.5 $mg \cdot kg^{-1}$ tracheal intubation was carried out using a Macintosh laryngoscope, blade #3 or 4. Severity of difficulty in intubation was estimated according to the view obtained at laryngoscopy [4] (arytenoids and/or glottis = easy; only epiglottis or not even epiglottis = difficult).

Homozygous thalassemia patients had a notable prevalence in the series studied (58/5,166; 1.1%); however, it was not indicative of the general population [5], as our hospital is a referral center for the disease. It is widely accepted that hemoglobin levels are inversely correlated with maxilla size. According to our findings, the relative prevalence of patients with no evidence of hypertrophy of the maxilla was 26/58 (44.8%), reflecting the effectively followed-up homozygous thalassemia patients. Statistical analysis revealed a highly significantly increased risk of difficult intubation amongst patients presented with hypertrophy of maxilla due to thalassemia, as compared to patients with no evidence of any risk factor (Table I, probability of difficulty: 18.8% vs. 0.9%, two-tailed P-value = 0.0017, Fisher's exact test; relative risk: 20.7, $9.5 < RR < 45.2$, 95% Taylor series confidence limits).

In conclusion, homozygous thalassemia, when accompanied by maxillary deformity, constitutes an aggravating factor for difficult intubation. It proved to be of statistically equal strength when compared to traditionally recognised risk factors (Table I).

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